

Fig. 1

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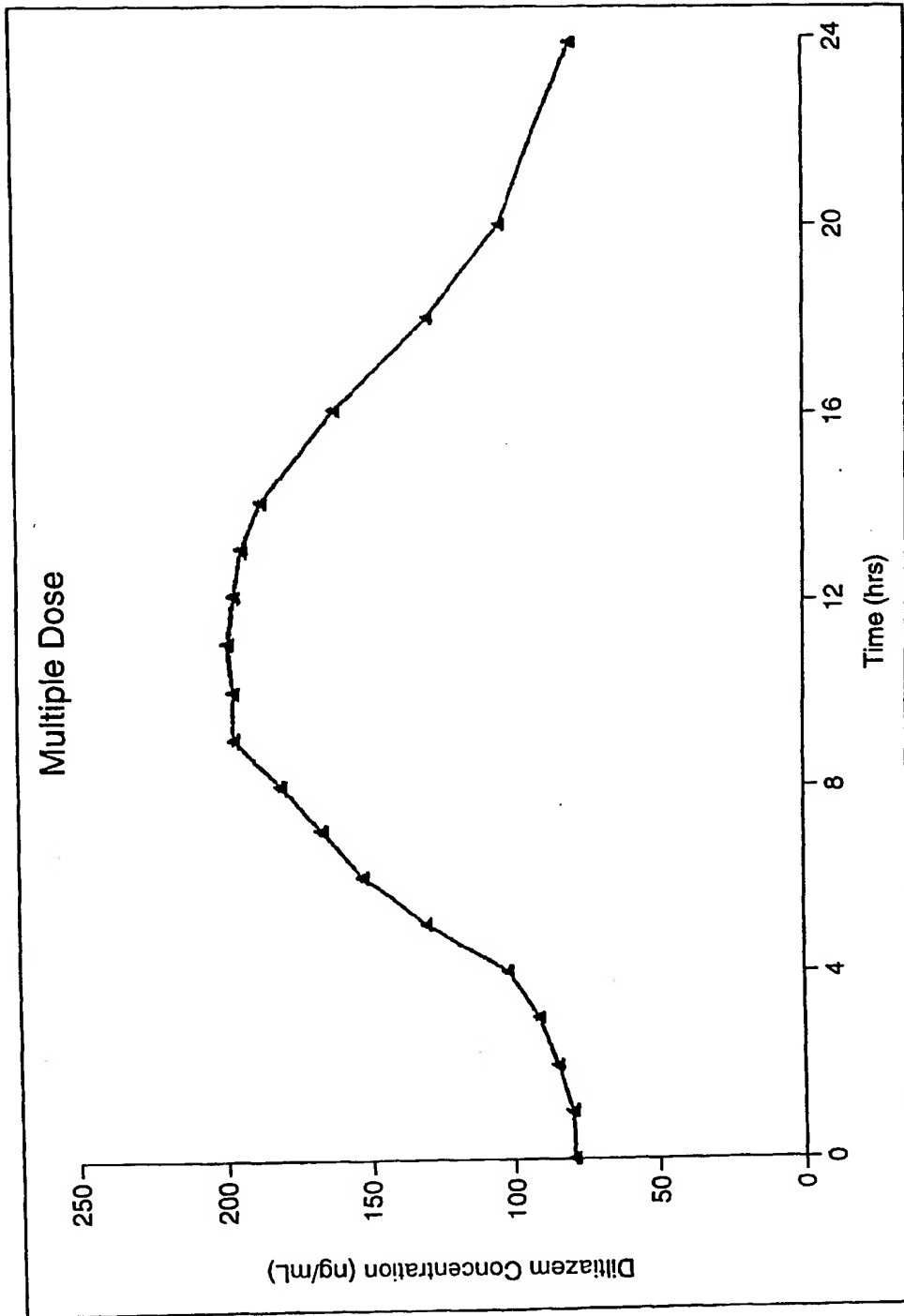


Fig. 2

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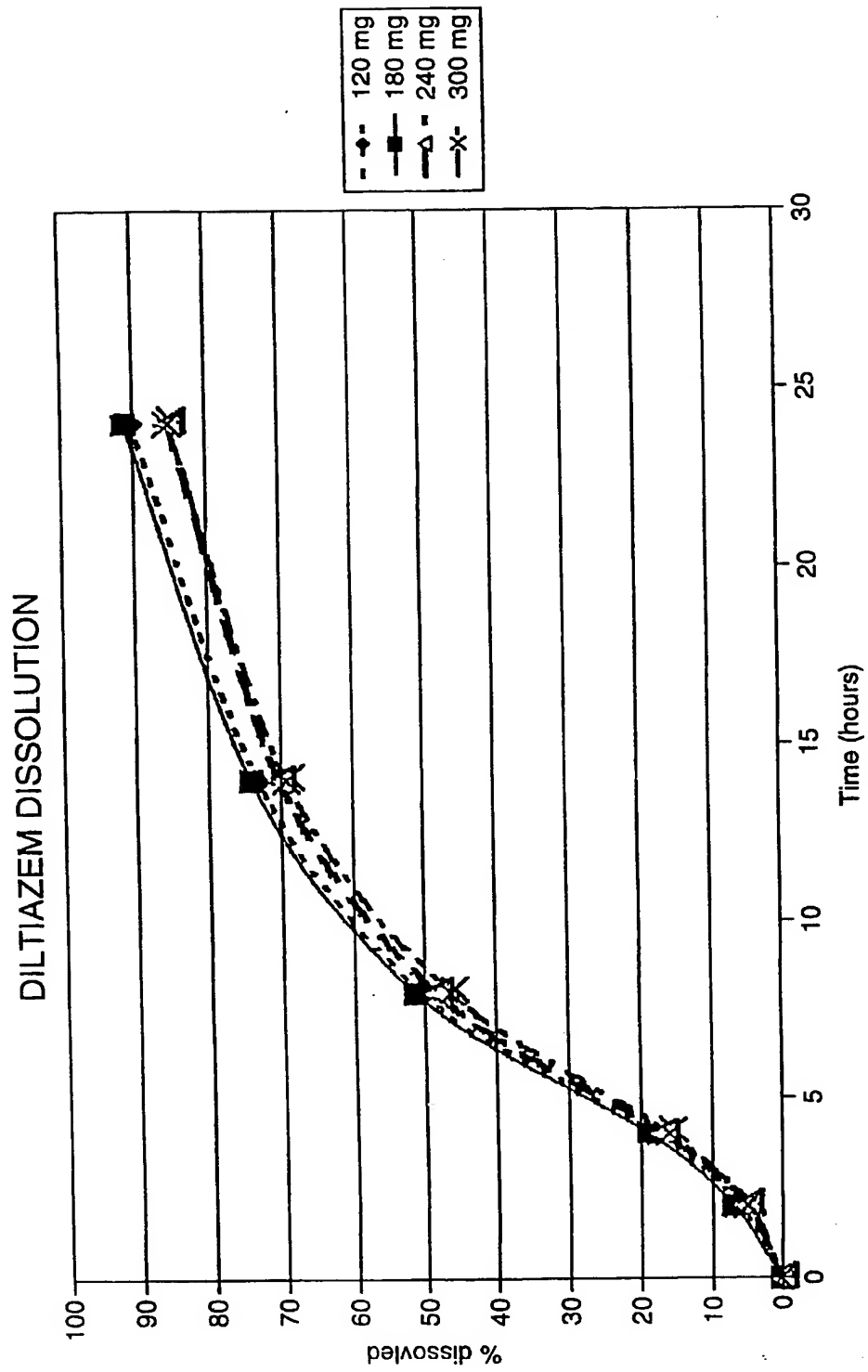


Fig. 3

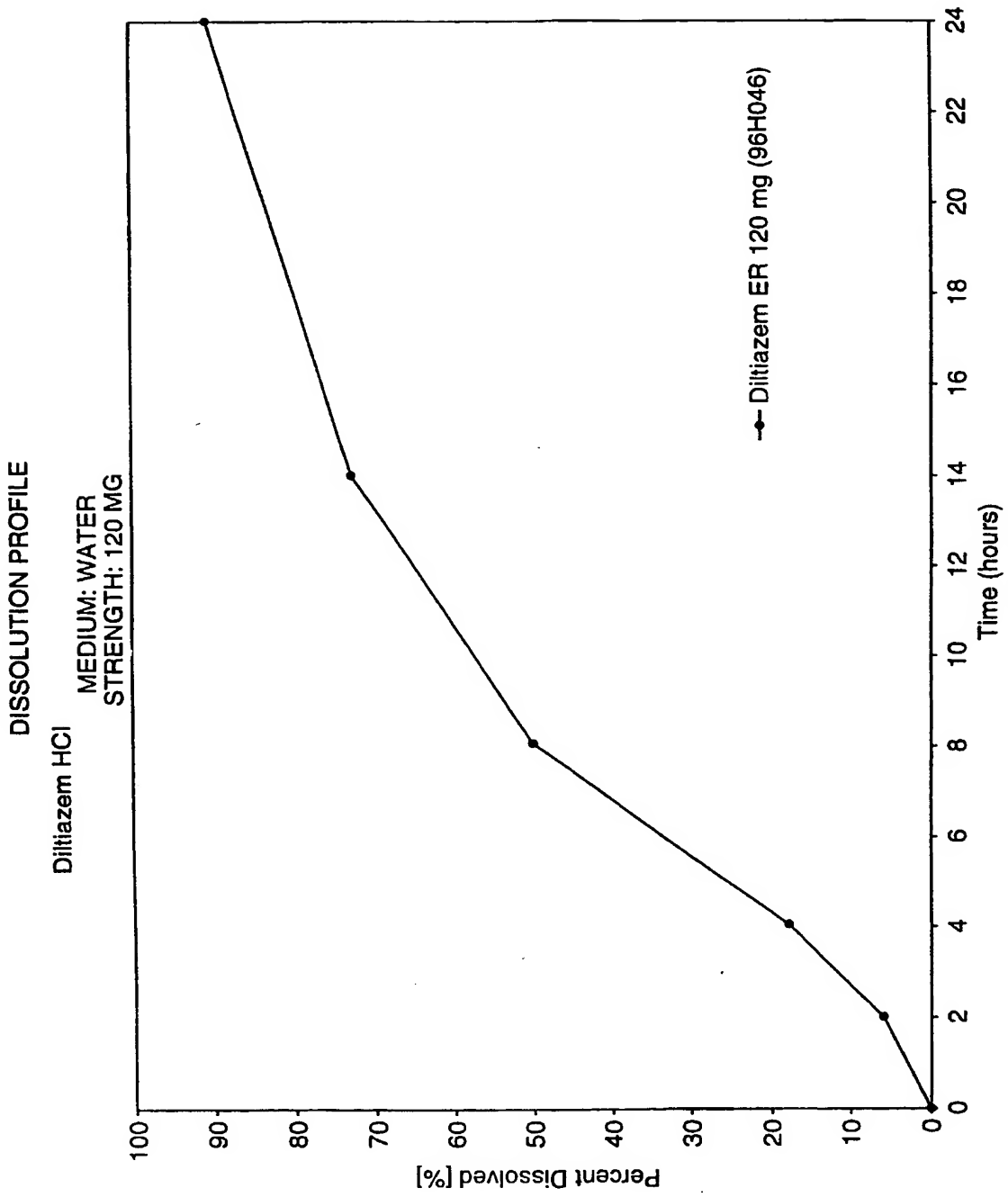


Fig. 4

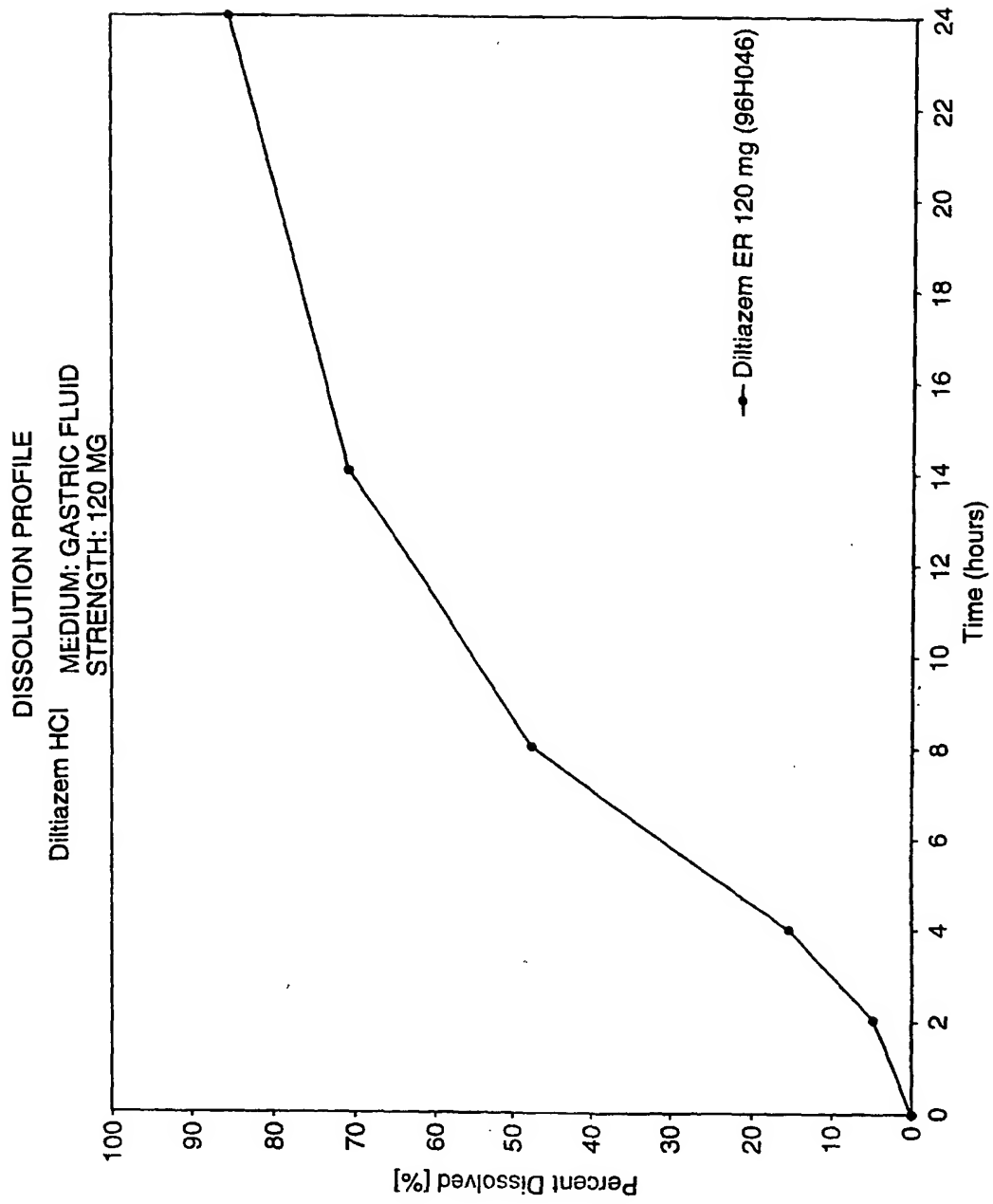


Fig. 5

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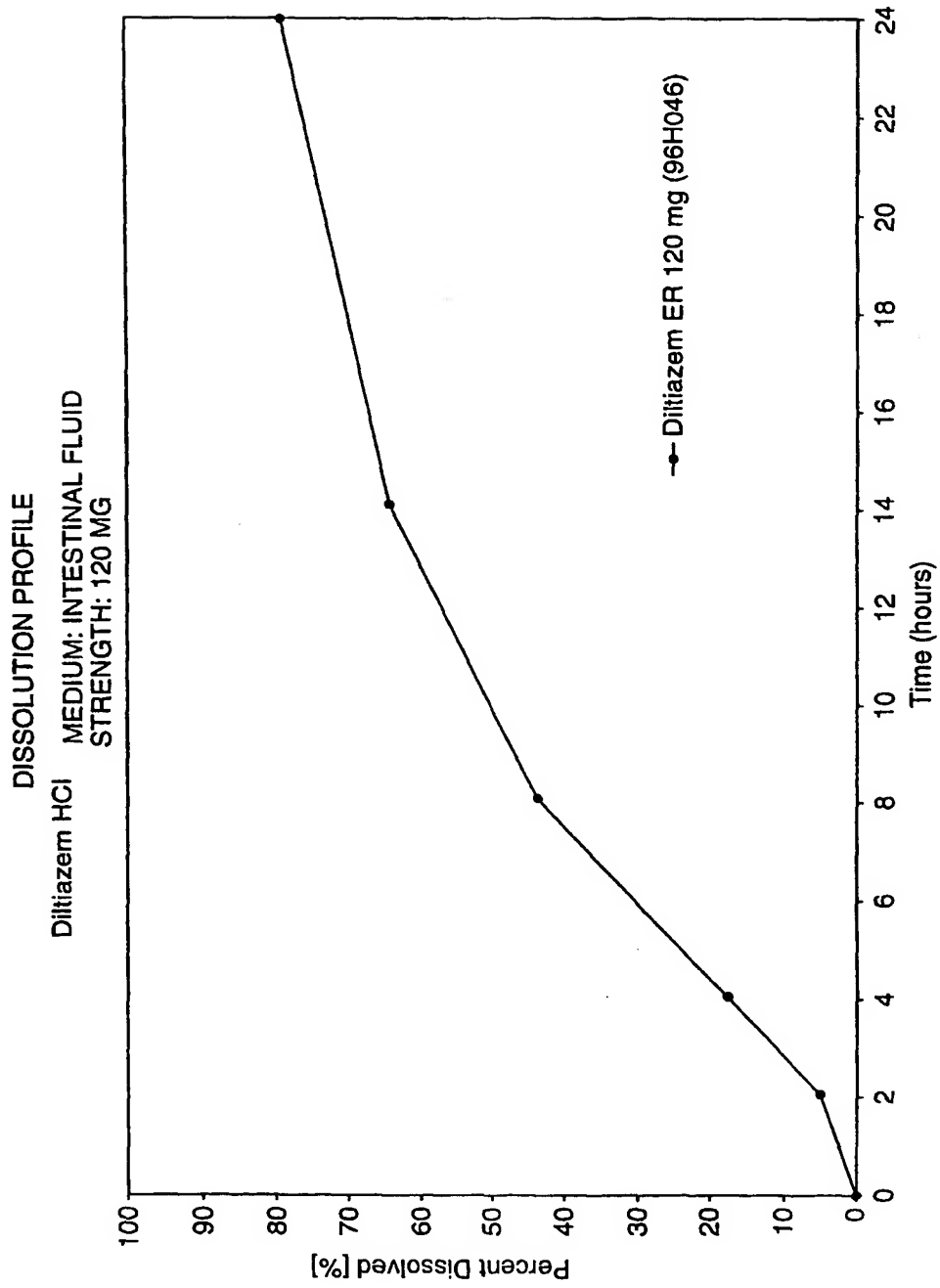


Fig. 6

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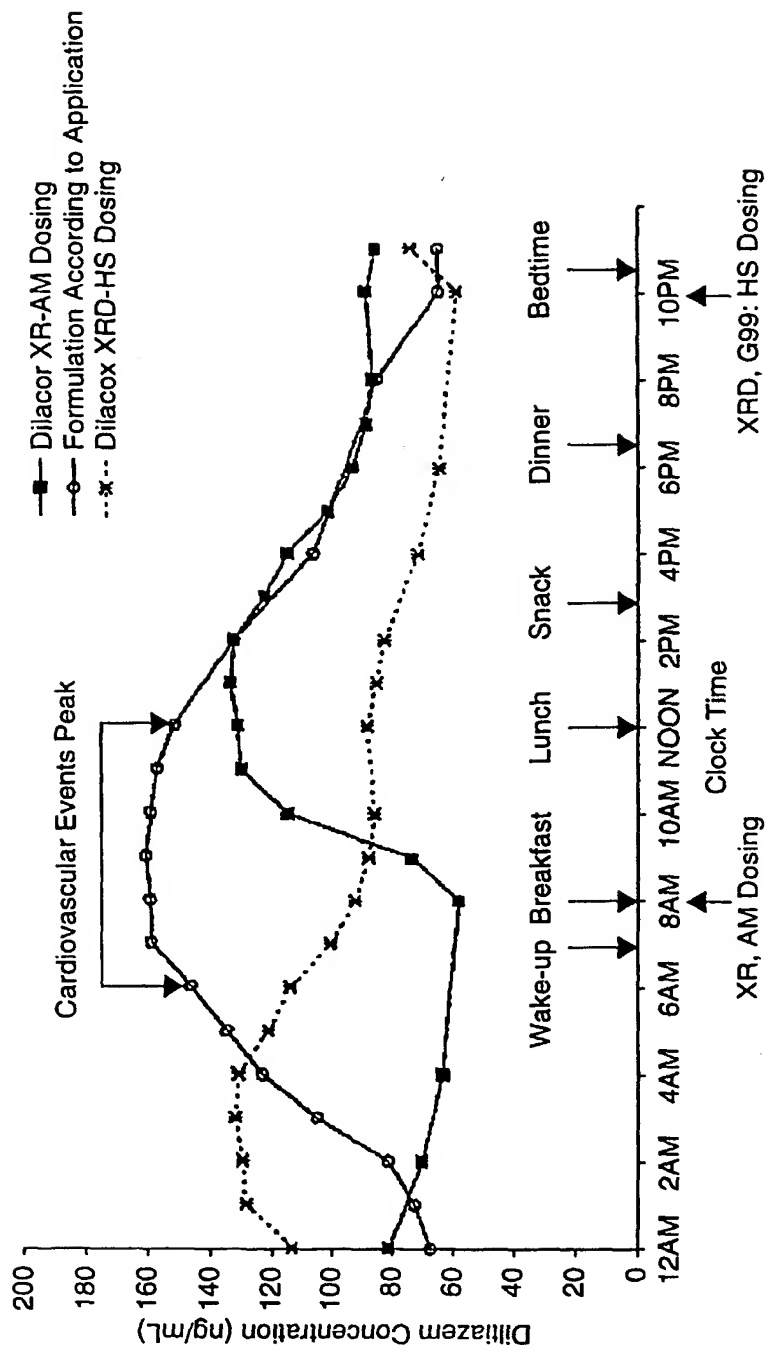


Fig. 7

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■ Tiazac
○ Formulation
According to
Application

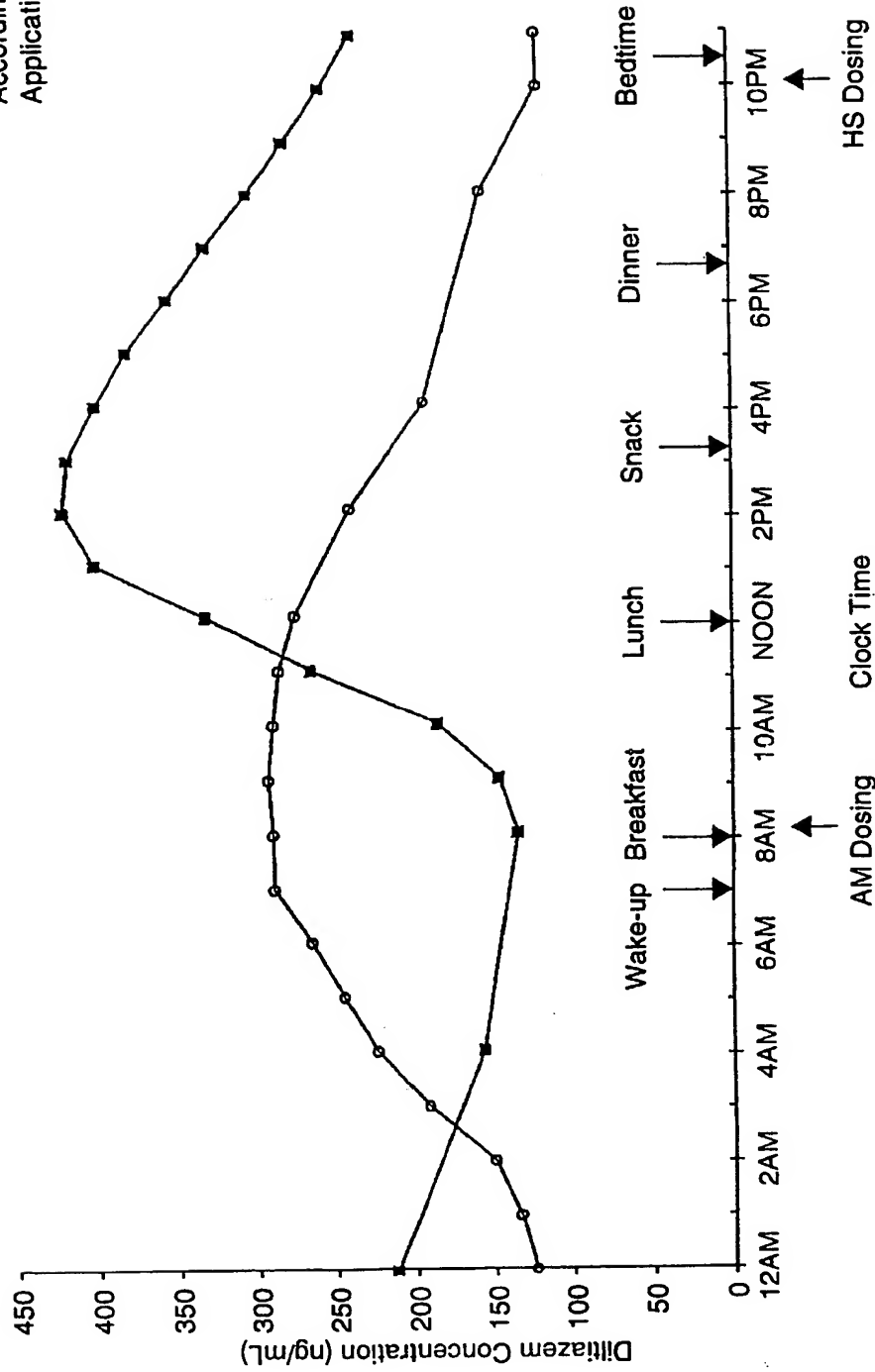


Fig. 8

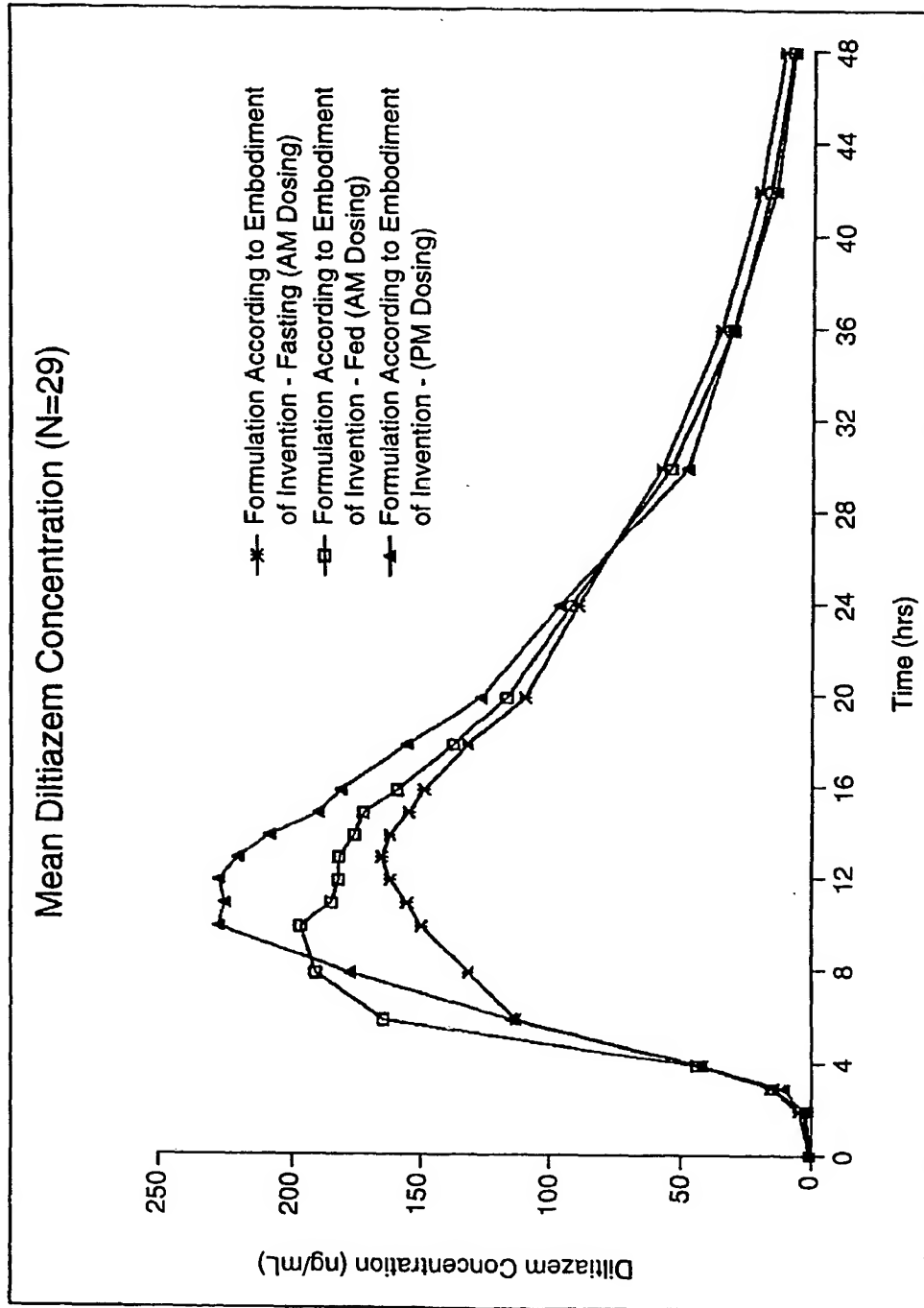


Fig. 9

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Diltiazem AUCt PK Summary

Formulation According to Embodiment of Invention

Subject	Morning Fasting		Morning Fed		Night Dosing		Morning	Night/Morning
	AUCt	Log AUCt	AUCt	Log AUCt	AUCt	Log AUCt	Fed/Fast	
2	1730.75	7.46	2647.15	7.88	1987.11	7.59	1.53	1.15
3	2712.98	7.91	2336.67	7.76	3248.94	8.09	0.86	1.20
4	2688.34	7.90	1907.61	7.55	2892.21	7.97	0.71	1.08
5	4192.37	8.34	4108.85	8.32	4702.33	8.46	0.98	1.12
6	3074.51	8.03	2887.98	7.97	3900.06	8.27	0.94	1.27
7	1629.81	7.40	1847.56	7.52	2723.36	7.91	1.13	1.67
8	941.10	6.85	1970.97	7.59	1835.11	7.51	2.09	1.95
9	3144.13	8.05	3462.59	8.15	2923.86	7.98	1.10	0.93
10	2074.94	7.64	2997.45	8.01	4028.83	8.30	1.44	1.94
11	3653.96	8.20	2771.53	7.93	3464.72	8.15	0.76	0.95
12	2684.22	7.90	3790.43	8.24	3141.47	8.05	1.41	1.17
13	3352.69	8.12	3751.95	8.23	3708.83	8.22	1.12	1.11
14	2988.61	8.00	3665.60	8.21	3141.05	8.05	1.23	1.05
15	6796.97	8.82	8204.22	9.01	7578.33	8.93	1.21	1.11
16	2873.70	7.96	4644.79	8.44	4192.09	8.34	1.62	1.46
17	4468.33	8.40	4222.55	8.35	3762.50	8.23	0.94	0.84
18	5654.29	8.64	5635.72	8.64	7159.38	8.88	1.00	1.27
19	4944.07	8.51	5107.44	8.54	4812.20	8.48	1.03	0.97
20	2986.73	8.00	2988.34	8.00	2791.23	7.93	1.00	0.93
21	2908.88	7.98	3314.12	8.11	4389.98	8.39	1.14	1.51
22	4270.43	8.36	3790.06	8.24	3631.01	8.20	0.89	0.85
23	6150.18	8.72	6092.56	8.71	7478.22	8.92	0.99	1.22
25	2926.46	7.98	5633.64	8.64	4839.10	8.48	1.93	1.65
26	3928.61	8.28	4614.43	8.44	4359.77	8.38	1.17	1.11
27	3637.94	8.20	4587.48	8.43	4063.15	8.31	1.26	1.12
28	4177.76	8.34	4945.31	8.51	6689.14	8.81	1.18	1.60
29	3609.69	8.19	2720.67	7.91	2163.20	7.68	0.75	0.60
30	4483.17	8.41	5222.54	8.56	5587.50	8.63	1.16	1.25
32	4058.04	8.31	3531.47	8.17	3082.87	8.03	0.87	0.76
Mean	3542.88	8.10	3910.40	8.21	4078.57	8.25	1.15	1.20
SD	1304.23	0.41	1431.24	0.36	1554.69	0.37	0.33	0.33
CV	36.81	5.08	36.60	4.43	38.12	4.46	28.23	27.33
Median	3352.69	8.12	3751.95	8.23	3762.50	8.23	1.12	1.12
Geo Mean	3292.83	8.09	3671.24	8.20	3818.30	8.24	1.11	1.16

Fed/Fasting Ratio (Morning Dosing)

Ratio of Means	1.10	#
Ratio of Geo Means	1.11	#
Avg of Individual Ratios	1.15	#

Night/Morning Ratio

Ratio of Means	1.15
Ratio of Geo Means	1.16
Avg of Individual Ratios	1.20

Fig. 9A

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Diltiazem Cmax PK Summary

Formulation According to Embodiment of Invention

Subject	Morning Fasting			Morning Fed			Night Dosing			Morning	
	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	Fed/Fast Ratio	Night/Morning Ratio
2	10.0	98.63	4.59	10.0	187.71	5.23	13.0	143.84	4.97	1.90	1.48
3	13.0	136.18	4.91	11.0	123.04	4.81	10.0	246.57	5.51	0.90	1.81
4	15.0	133.23	4.89	10.0	118.68	4.78	10.0	191.44	5.25	0.89	1.44
5	8.0	222.52	5.41	8.0	185.68	5.28	12.0	254.98	5.54	0.88	1.15
6	12.0	150.95	5.02	8.0	164.11	5.10	16.0	178.67	5.19	1.09	1.19
7	10.0	90.68	4.51	14.0	121.64	4.80	12.0	179.87	5.19	1.34	1.98
8	8.0	85.68	4.18	11.0	119.30	4.78	11.0	133.35	4.89	1.82	2.03
9	13.0	155.46	5.05	6.0	292.70	5.88	12.0	175.62	5.17	1.88	1.13
10	8.0	95.45	4.56	6.0	168.91	5.12	13.0	196.94	5.28	1.75	2.06
11	14.0	212.41	5.36	11.0	154.64	5.04	14.0	183.66	5.21	0.73	0.86
12	10.0	117.75	4.77	10.0	201.43	5.31	11.0	174.95	5.16	1.71	1.49
13	14.0	149.90	5.01	13.0	188.51	5.24	10.0	208.76	5.34	1.26	1.39
14	13.0	139.54	4.94	6.0	205.35	5.32	13.0	187.32	5.23	1.47	1.34
15	16.0	268.48	5.59	15.0	330.93	5.80	13.0	450.34	6.11	1.24	1.89
16	13.0	134.55	4.90	8.0	281.74	5.64	10.0	236.10	5.48	2.09	1.75
17	12.0	224.85	5.41	10.0	244.82	5.50	14.0	203.51	5.32	1.09	0.91
18	14.0	281.88	5.64	8.0	308.25	5.73	13.0	479.11	6.17	1.09	1.70
19	15.0	227.89	5.43	11.0	262.82	5.57	13.0	231.49	5.44	1.15	1.02
20	14.0	137.54	4.82	10.0	175.76	5.17	10.0	173.93	5.16	1.28	1.26
21	13.0	164.75	5.10	13.0	197.63	5.29	13.0	301.72	5.71	1.20	1.83
22	16.0	182.52	5.21	11.0	207.19	5.33	10.0	247.08	5.51	1.14	1.35
23	18.0	269.97	5.60	10.0	340.21	5.83	10.0	500.82	6.22	1.28	1.86
25	10.0	166.06	5.11	8.0	322.55	5.78	10.0	263.27	5.57	1.94	1.59
26	13.0	208.19	5.34	10.0	237.50	5.47	10.0	235.12	5.46	1.14	1.13
27	10.0	162.47	5.09	8.0	255.85	5.54	10.0	170.18	5.14	1.57	1.05
28	13.0	218.59	5.39	11.0	236.10	5.46	11.0	384.02	5.95	1.08	1.76
29	13.0	215.15	5.37	13.0	160.73	5.08	12.0	129.94	4.87	0.75	0.60
30	14.0	242.68	5.49	12.0	244.58	5.50	10.0	338.64	5.82	1.01	1.39
32	12.0	303.43	5.72	15.0	204.09	5.32	11.0	231.33	5.44	0.67	0.76
Mean	12.6	176.45	5.12	10.2	215.53	5.33	11.6	242.48	5.42	1.29	1.41
SD	2.5	61.85	0.37	2.5	64.85	0.31	1.8	98.98	0.38	0.40	0.39
CV	19.8	34.66	7.32	24.3	30.09	5.83	14.1	40.82	6.58	30.89	27.83
Median	13.0	164.75	5.10	10.0	204.09	5.32	11.0	208.76	5.34	1.20	1.39
Geo Mean	12.3	167.47	5.11	9.9	206.00	5.32	11.5	226.83	5.41	1.23	1.35
Fed/Fasting Ratio (Morning Dosing)											Night/Morning Ratio
Ratio of Means											1.36
Ratio of Geo Means											1.35
Avg of Individual Ratios											1.41

Fig. 9B

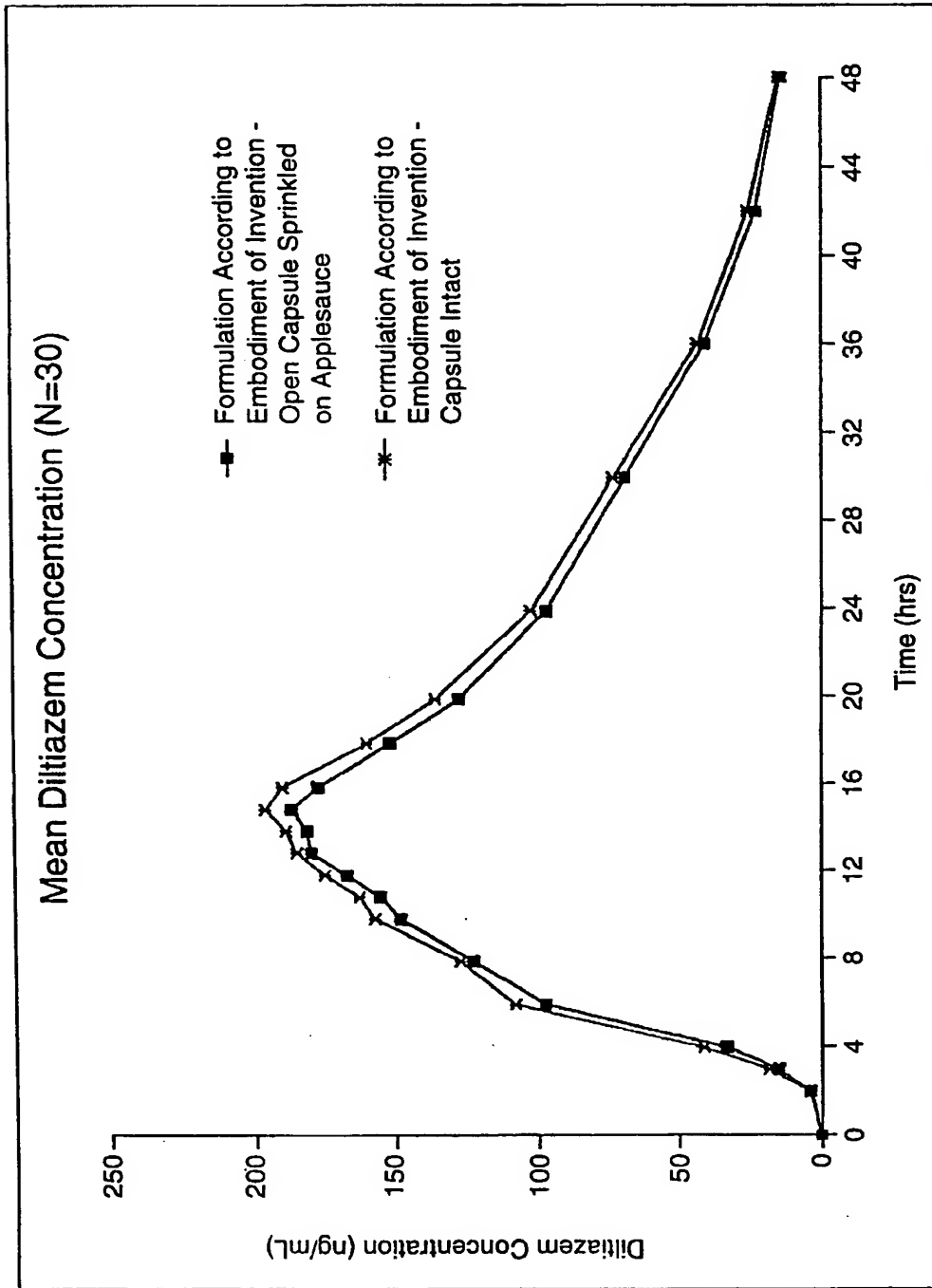


Fig. 10

PK Summary (N=30)

Diltiazem PK

Open Capsule Sprinkled on Applesauce / Capsule Intact

AUCt

Ratio of Means % 94.16
 Ratio of Geo Means % 93.98
 Avg of Individual Ratios % 96.03
 90% C.I. 88%-99%
 Intra-CV 13.47%

Cmax

Ratio of Means % 93.35
 Ratio of Geo Means % 93.00
 Avg of Individual Ratios % 95.73
 90% C.I. 86%-99%
 Intra-CV 16.07%

Imax

Open Capsule Sprinkled on Applesauce
 Capsules Intact

Mean

13.7 hours
 13.5 hours

Fig. 10A

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Diltiazem AUCt Results

Formulation According to Embodiment of Invention

Subject	Open Capsules Sprinkled on Applesauce (A)		Capsule Intact (B)		(A:B) Ratio
	AUCt	Log Cmax	AUCt	Log Cmax	
1	3937.18	8.28	3251.62	8.09	1.21
2	3792.89	8.24	5502.18	8.61	0.69
3	1616.35	7.39	2358.22	7.77	0.69
4	8209.44	9.01	7954.29	8.98	1.03
5	2171.26	7.68	2452.78	7.80	0.89
6	5710.90	8.65	7082.30	8.87	0.81
7	1983.56	7.59	2624.03	7.87	0.76
8	3862.46	8.26	3114.53	8.04	1.24
9	6069.65	8.71	4585.60	8.43	1.32
10	3907.33	8.27	6393.14	8.76	0.61
11	3842.58	8.25	4292.30	8.36	0.90
12	4873.82	8.49	6493.87	8.78	0.75
13	2707.85	7.90	3922.90	8.27	0.69
14	2553.27	7.85	2159.88	7.68	1.18
15	2042.47	7.62	2902.70	7.97	0.70
16	4650.14	8.44	4769.32	8.47	0.98
17	3705.72	8.22	3464.89	8.15	1.07
19	7881.69	8.97	6851.45	8.83	1.15
21	6151.00	8.72	6292.65	8.75	0.98
22	2138.64	7.67	1933.52	7.57	1.11
23	3983.50	8.29	5177.74	8.55	0.77
24	3939.51	8.28	3517.56	8.17	1.12
25	2318.36	7.75	2016.26	7.61	1.15
27	2061.09	7.63	1928.02	7.56	1.07
28	2871.31	7.96	3312.87	8.11	0.87
29	4305.14	8.37	3559.57	8.18	1.21
30	3190.17	8.07	3565.88	8.18	0.89
31	3422.16	8.14	3012.17	8.01	1.14
33	4906.47	8.50	5206.52	8.56	0.94
34	2969.19	8.00	3255.28	8.09	0.91
Mean	3859.17	8.17	4098.47	8.24	0.96
SD	1664.90	0.42	1708.24	0.41	0.20
CV	43.14	5.10	41.68	5.03	20.69
Median	3817.74	8.25	3538.57	8.17	0.96
Geo Mean	3546.16	8.16	3773.43	8.23	0.94
Test/Ref Ratio					
Ratio of Means %		94.16			
Ratio of Geo Means %		93.98			
Avg of Individual Ratios		0.96			
90% C.I.		88%-99%			
Intra-CV		13.47%			

Fig. 10B

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Diltiazem Cmax Results

Formulation According to Embodiment of Invention

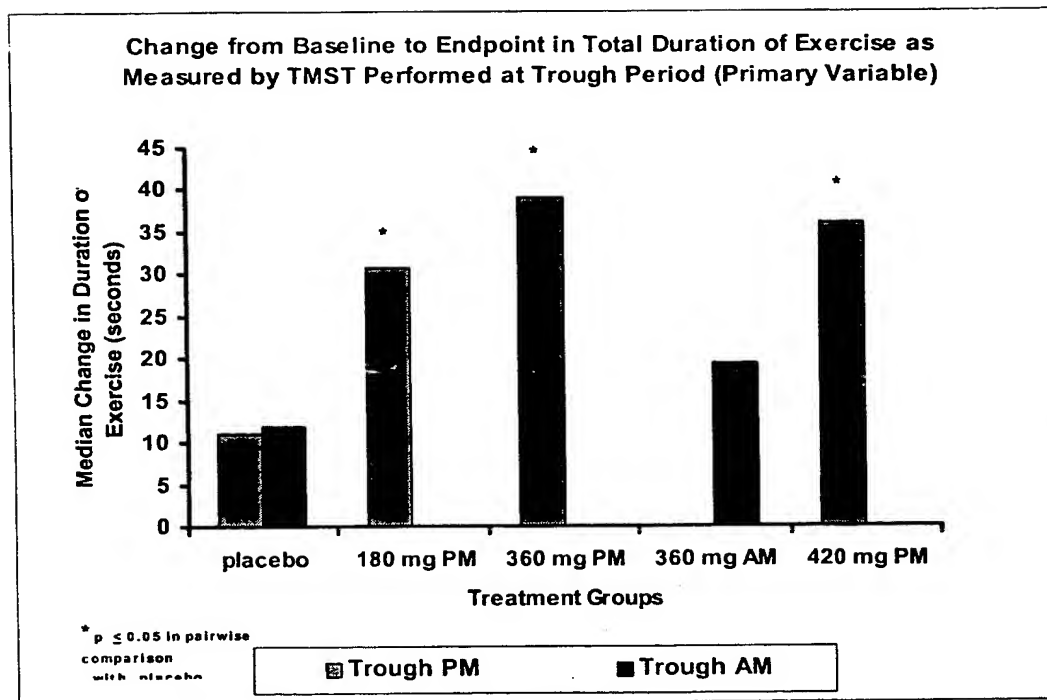
Subject	Open Capsule Sprinkled on Applesauce (A)			Capsule Intact (B)			(A:B) Ratio
	Tmax	Cmax	Log Cmax	Tmax	Cmax	Log Cmax	
1	13.0	184.35	5.22	13.0	228.99	5.43	0.81
2	14.0	192.44	5.26	12.0	286.72	5.66	0.67
3	13.0	103.87	4.64	12.0	127.07	4.84	0.82
4	10.0	372.93	5.82	8.0	298.05	5.70	1.25
5	14.0	107.71	4.68	16.0	147.84	5.00	0.73
6	13.0	244.87	5.50	15.0	315.48	5.75	0.78
7	14.0	115.23	4.75	16.0	135.27	4.91	0.85
8	13.0	257.26	5.55	15.0	179.11	5.19	1.44
9	8.0	232.12	5.45	10.0	194.37	5.27	1.19
10	16.0	172.20	5.15	15.0	281.81	5.64	0.61
11	13.0	177.41	5.18	8.0	181.17	5.20	0.98
12	13.0	225.55	5.42	10.0	327.23	5.79	0.69
13	15.0	135.86	4.91	15.0	213.37	5.36	0.64
14	15.0	154.65	5.04	14.0	135.94	4.91	1.14
15	12.0	114.81	4.74	15.0	181.80	5.20	0.63
16	15.0	294.21	5.68	13.0	296.58	5.69	0.99
17	15.0	187.32	5.23	15.0	183.62	5.21	1.02
19	16.0	385.36	5.95	15.0	376.57	5.93	1.02
21	15.0	318.06	5.76	10.0	276.15	5.62	1.15
22	14.0	114.40	4.74	14.0	97.24	4.58	1.18
23	12.0	260.20	5.56	12.0	346.74	5.85	0.75
24	14.0	211.61	5.35	16.0	202.88	5.31	1.04
25	14.0	155.98	5.05	15.0	125.66	4.83	1.24
27	16.0	79.66	4.38	16.0	67.35	4.21	1.18
28	16.0	124.76	4.83	16.0	165.01	5.11	0.76
29	15.0	225.58	5.42	10.0	164.02	5.10	1.38
30	14.0	166.54	5.12	15.0	165.41	5.11	1.01
31	15.0	134.14	4.90	14.0	135.19	4.91	0.99
33	13.0	282.10	5.64	16.0	275.33	5.62	1.02
34	10.0	118.88	4.78	15.0	155.15	5.04	0.77
Mean	13.7	195.00	5.19	13.5	208.90	5.27	0.96
SD	1.9	80.09	0.41	2.5	80.27	0.41	0.23
CV	13.8	41.07	7.83	18.3	38.43	7.73	24.25
Median	14.0	180.88	5.20	15.0	182.71	5.21	0.99
Geo Mean	13.5	180.09	5.18	13.3	193.65	5.25	0.83
Test/Ref Ratio							
Ratio of Means %			93.35				
Ratio of Geo Means %			93.00				
Avg of Individual Ratios			0.96				
90% C.I.			86%-99%				
Intra-CV			16.07%				

Fig. 10C

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FIGURE 11



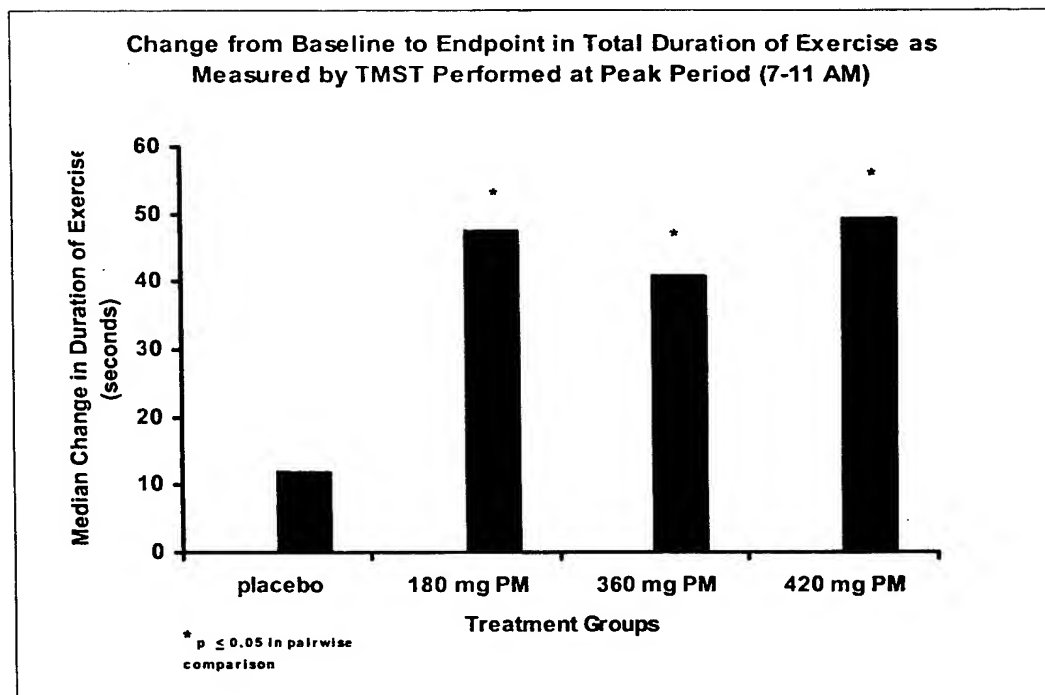
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FIGURE 12

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FIGURE 13

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